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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/068,569	02/06/2002	Emad S. Alnemri	480140.475	8367

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EXAMINER

KOSAR, ANDREW D

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 08/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/068,569	ALNEMRI, EMAD S.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-31 and 90 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 23-31 and 90 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 February 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>5/2/02</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims 23-31 and 90 are pending in the instant application. Claims 23-31 and 90 are rejected.

Preliminary Amendment

The preliminary amendment filed on May 8, 2002 is acknowledged, wherein claims 1-22, 32-89, and 91-94 are cancelled and claims 23-31 and 90 are amended.

Priority

Applicants claim to the benefit of priority to provisional application 60/267,966, and as a CIP to application 09/939,293 is noted in the application data sheet.

Drawings

The drawings are objected to because Figures 6, 8, and 19 are dark images. Corrected drawing sheets are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the

changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Figures 1-20 in the instant application, filed on February 6, 2002 and the figures were published in the journal Nature, March 2001, should be designated by a legend such as --Prior Art-- because only that which is old is illustrated. See MPEP § 608.02(g). Corrected drawing sheets are required in reply to the Office action to avoid abandonment of the application. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because the detailed description of the drawings does not accurately describe Figure 9. Figure 9 illustrates nine "SEQ ID NO:", however Applicant has failed to identify "Omi" and "Veto" in the description as SEQ ID NO:9 and SEQ ID NO:10, as included in the sequence listing. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claim 90 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative form only, i.e.-

"...of any one of claims 23-31..." See MPEP § 608.01(n). Appropriate correction is required.

Claim 90 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim is drawn to any of the peptides of Claims 23-31 and a physiological acceptable carrier, however the specification does not provide guidance as to what the carrier should be. Therefore, the peptide, itself can be the carrier, and thus the claim is not further limiting.

Examiner Notes

Herein, citations to relevant passages of U.S. Patents are as (Column #: line #), i.e.- (c3:1+). For applications, foreign patents, and non-patent literature it is as (Page #), i.e.- (p1), and when applicable (Page #: line or paragraph #), i.e.- (p1:4 or p1:p4).

The Examiner notes that SEQ ID NO:6 and 11 are the same sequence.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 23-31 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Because of the breadth of the claims, "A peptide or polypeptide comprising at least an amino acid sequence set forth in SEQ ID NO:13..." the claim reads upon any peptide or polypeptide with SEQ ID NO:13, such as

proteins. Proteins which have not been isolated are products of nature, and thus are non-statutory matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-31 and 90 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant application shares a common inventor/author and common subject matter with that of Srinivasula, et al^a. The Western blot presented as Figure 2b in Srinivasula (Figure 6 in the instant application), has been found to have been falsified through an inquiry by the U.S. Department of Health and Human Services, the findings of which were published as Federal Register 01-12681 "Finding of Scientific Misconduct"^b. The findings state in part, "PHS finds that Dr. Saleh falsified: ... (E) Figure 2b, the panel that shows a Western blot of Casp-9(WT) in ... Nature 410(6824):112-116,2001. The Figure 2b data were actually taken from a Western blot of Bcl-XL..." Absent evidence to the contrary, the specification is not enabling.

^a SM Srinivasula, et al. A conserved XIAP-interaction motif in caspase-9 and Smac/DIABLO regulates caspase activity and apoptosis. Nature (2001), 410, 112-116.

^b FR Doc. 01-12681. Federal Register. May 21, 2001. Vol 66, No 98 p 27974-27975.

Claims 28-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 28-31 each recite, "a variant thereof" which can be interpreted as, "any variant thereof". "A variant thereof" is not defined in the specification or the claims in such a way that a skilled artisan would not be reasonably apprised of the metes and bounds of the claimed invention. While the specification teaches how to choose a variant, stating that "[g]uidance in determining which amino acid residues can be substituted, inserted, or deleted without abolishing biological or immunological activity can be found using computer programs..." (p27), the application does not disclose a representative number of species to show applicant was in possession of "any variant thereof".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 recites the limitation "said BIR" of claim 23. There is insufficient antecedent basis for this limitation in the claim. It appears that Claim 25 depends more appropriately from claim 24 which recites, "... at least one BIR domain."

Claim 27 recites, "... selected from the group consisting of the first four amino acid residues of each of SEQ ID NO:2... and SEQ ID NO:10." The claim is confusing and, therefore, indefinite. The claim reads initially as a Markush group (selected from the group), however it then recites as if requiring all of the components with the limitation, "of each of". It is unclear what the metes and bounds of the claimed invention comprise, and thus the claim is indefinite.

Claim 27 recites "SEQ ID NO:3, ...SEQ ID NO:5, ... and SEQ ID NO:10." There is insufficient antecedent basis for the limitations of SEQ ID NO: 3, 5, or 10 in the claim from which it depends, specifically SEQ ID NO:13. SEQ ID NO:13 does not provide for AA4₄ to be phenylalanine (Phe or F) and thus lacks proper antecedent basis.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23-27, 29 and 30 are rejected under 35 U.S.C. 102(a) as being anticipated by Liu, et al ^c.

The instant claims are directed towards a peptide or polypeptide comprising at least an amino acid sequence of SEQ ID NO:13, A[VTI][PA][GAVLIPSTCMNQ]^d which binds at least a portion of an IAP (*Claim 23*), wherein said portion is at least one BIR domain (*Claim 24*), wherein said BIR is BIR3 (*Claim 25*)^e. The binding may also be to a

^c Z Liu, et al. Structural basis for binding of Smac/DIABLO to the XIAP BIR3 domain. Nature (2000), 408, 1004-1008.

^d The braces are used to indicate a selection of multiple peptides at the residue position. For Example, amino acid position 3 may be either P or A.

^e As interpreted by the Examiner, see 112 2nd rejection.

full length IAP (*Claim 26*). The peptide or polypeptide may further be limited to at least the first 4 amino acid residues of any one of SEQ ID NO:2-10 (*Claim 27*).

Similarly, The instant claims are directed towards a peptide or polypeptide comprising at least an amino acid sequence of SEQ ID NO:15 or 12, or variants thereof, which binds at least a portion of an IAP (*Claims 29 and 30, respectively*).

Liu teaches peptides comprising the sequence of SEQ ID NO:13, *supra*, and at least the first 4 amino acids of SEQ ID NO:2-4 and 8 (p1005, Figure 1b and p1007, Table 1). Because the specification of the instant claims states that SEQ ID NO:13 is the “consensus IAP-binding sequence” (p6), it is the Examiners position that it is the only requirement set forth for identifying whether a peptide will bind IAP, specifically BIR, or more specifically BIR3. Absent evidence to the contrary, the peptides of Table 1 and Figure 1b would necessarily bind “at least a portion” and subsequently “a full length IAP”, because no additional requirement is set forth in the specification to determine that more recognition is required to bind a full length sequence. Because of the reasons stated, Liu anticipates Claims 23-27.

Liu teaches a peptide comprising a variant of SEQ ID NO:15 (AVPY) in Table 1 (AVPIA-NH₂), anticipating Claim 29. Liu also teaches a peptide comprising SEQ ID NO:12 (AVPIAQK) in Figure 1b and Table 1(AVPIAQKSE), anticipating Claim 30.

Claims 23-28 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Seol, et al^f.

^f D-W Seol, et al. A caspase-9 variant missing the catalytic site is an endogenous inhibitor of apoptosis. Journal of Biological Chemistry (1999), 274(4), 2072-2076.

The instant claims are described *supra*. The instant claims are directed towards a peptide or polypeptide comprising at least an amino acid sequence of SEQ ID NO:11, or variants thereof, which binds at least a portion of an IAP (*Claim 28*). The instant claims are also directed towards a peptide or polypeptide comprising a first portion which binds at least a portion of IAP and a second portion of procaspase-9 which binds at least a portion of IAP but lacks cysteine protease activity, or a variant thereof (*Claim 31*).

Seol teaches caspase-9 and caspase-9S (p2073, Figure 1a) which meets all of the limitations of Claims 23-28, and 31. Caspase-9 and caspase-9S possess SEQ ID NO:11 and 13 (ATPFQEGLRTFDQLD), which also reads upon SEQ ID NO: 4 and 6. Caspase-9S lacks the catalytic domain (p2073, Figure 1a caption), and is therefore considered 'mutated' as required in the instant claims (*Claim 31*) and has the requisite 'first portion' variant thereof (ALPL) and the requisite 'second portion' (ATPFQ). As recited in the 102(a) rejection, *supra*, absent evidence to the contrary, the polypeptides of Figure 1a would necessarily bind "at least a portion" and subsequently "a full length IAP", because no additional requirement is set forth in the specification to determine that more recognition is required to bind a full length sequence. Because of the reasons stated, Seol anticipates Claims 23-28 and 31.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 23-27, 29, 30, and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu.

Claim 90 is directed towards a composition of any of the peptides of Claims 23-31 and a physiological carrier.

The teachings of Liu are *supra*. Liu does not teach a physiologically carrier.

As stated in the Claims Objections, *supra*, a physiologically acceptable carrier is not defined in the specification, and therefore a teaching of any of the peptides of any of the claims reads upon the limitation "...and a physiologically acceptable carrier".

Further, it is well within the purview of the skilled artisan to place the peptide in aqueous media, such as water, for reconstituting lyophilized protein. For these reasons and those *supra*, claim 90 is obvious in view of Liu.

Claims 23-28, 31, and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seol.

The instant claims are *supra*.

The teachings of Seol are *supra*. Seol does not teach a physiologically carrier.

As stated in the Claims Objections, *supra*, a physiologically acceptable carrier is not defined in the specification, and therefore a teaching of any of the peptides of any of the claims reads upon the limitation "...and a physiologically acceptable carrier".


Further, it is well within the purview of the skilled artisan to place the peptide in aqueous media, such as water, for reconstituting lyophilized protein. For these reasons and those *supra*, claim 90 is obvious.

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 8am-430pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571)272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Andrew D. Kosar, Ph.D.
July 27, 2004

Patricia Leith
Primary Examiner
Art Unit 1654

